VELCADE (bortezomib)

**Line(s) of Business:**
HMO; PPO; QUEST Integration
Akamai Advantage

**Original Effective Date:**
03/09/2004

**Current Effective Date:**
05/01/2017

**Policy**

**A. Indications**

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**
- Treatment of patients with multiple myeloma
- Treatment of patients with mantle cell lymphoma

**Compendial Uses**
- **Active (symptomatic) multiple myeloma**
  - Primary therapy for active symptomatic myeloma or for disease relapse after 6 months following primary therapy with the same regimen in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and doxorubicin, dexamethasone and lenalidomide for transplant candidates, or dexamethasone and thalidomide for transplant candidates
  - Primary therapy in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide for nontransplant candidates
  - Maintenance therapy as monotherapy for active myeloma responding to primary therapy or for stable or responsive disease following stem cell transplant
  - Maintenance therapy as a single agent with tandem transplant for stable or responsive disease following autologous stem cell transplant
  - Therapy for previously treated myeloma for disease relapse or for progressive or refractory disease in patients who will not be treated with the same therapy as primary therapy
    - in combination with dexamethasone, dexamethasone and daratumumab, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide, or with dexamethasone and bendamustine
    - VTD-PACE (bortezomib, thalidomide, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide) regimen
    - In combination with pomalidomide and dexamethasone for patients who have received at least two prior therapies, including an immunomodulatory agent and a proteasome inhibitor, and have demonstrated disease
progression on or within 60 days of completion of the last therapy (preferred)
- In combination with liposomal doxorubicin
- In combination with elotuzumab and dexamethasone for patients who have received one to three prior therapies
- In combination with panobinostat and dexamethasone for patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

- Systemic light chain amyloidosis as a single agent or in combination with dexamethasone, dexamethasone and melphalan, or dexamethasone and cyclophosphamide
- Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as a single agent, or in combination with dexamethasone, rituximab, or rituximab and dexamethasone as primary therapy or therapy or previously treated disease that does not respond to primary therapy or for progressive or relapsed disease.
- Mantle cell lymphoma used for stage I-II disease, aggressive stage II bulky, III or IV disease, or symptomatic indolent stage II bulky, III or IV disease as
  - Less aggressive induction therapy with VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen
  - Second-line therapy with or without rituximab to achieve complete response to induction therapy or for relapsed, refractory or progressive disease
  - Second line therapy with bendamustine and rituximab to achieve complete response after partial response to induction therapy or for relapsed, refractory or progressive disease.
- Castleman’s disease
  - Subsequent therapy with or without rituximab for multicentric Castleman’s disease that has progressed following treatment of relapsed/refractory or progressive disease
  - Active (symptomatic) multiple myeloma
    Primary therapy in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and doxorubicin, dexamethasone and lenalidomide, or dexamethasone and thalidomide for stem cell transplant candidates
    Primary therapy in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide, or with melphalan and prednisone for non-transplant candidates
    Maintenance therapy as monotherapy
    Therapy for disease relapse after 6 months following primary therapy in patients who will be treated with the same regimen as primary therapy in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and doxorubicin, dexamethasone and lenalidomide, or dexamethasone and thalidomide for patients who were transplant candidates in combination with dexamethasone, dexamethasone and cyclophosphamide, dexamethasone and lenalidomide, or with melphalan and prednisone for patients who were non-transplant candidates
    Therapy for previously treated myeloma for disease relapse or for progressive or refractory disease in patients who will not be treated with the same therapy as primary therapy as a single-agent
in combination with dexamethasone, dexamethasone and lenalidomide, 
dexamethasone and cyclophosphamide, dexamethasone and thalidomide, 
liposomal doxorubicin, vorinostat, or as part of a combination regimen with 
dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and 
etoposide (VTD-PACE)
in combination with dexamethasone and panobinostat (Farydak) for patients who 
have received at least 2 prior regimens including bortezomib (Velcade) and an immunomodulatory agent 
Systemic light chain amyloidosis as a single agent or in combination with 
dexamethasone, dexamethasone and melphalan, or dexamethasone and 
cyclophosphamide
Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as a single agent, 
or in combination with dexamethasone, rituximab, or rituximab and dexamethasone
Mantle-cell lymphoma

Less aggressive induction therapy with VR-CAP (bortezomib, rituximab, 
cyclophosphamide, doxorubicin, and prednisone) regimen

Second-line therapy with or without rituximab for relapsed, refractory, or 
progressive disease

Castleman’s disease

Subsequent therapy with or without rituximab for multicentric Castleman’s disease 
that has progressed following treatment of relapsed/refractory or progressive 
disease

B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review:

- For members starting treatment: the patient’s treatment plan with treatment regimen including 
doctor, frequency, length of each cycle, number of cycles, and additional therapies (e.g., other 
medications, radiation) must be documented.
- For members continuing treatment: relevant laboratory reports, imaging studies, and office 
notes to substantiate status and progression of disease

C. PRESCRIBER RESTRICTION
The medication must be prescribed by, or in conjunction with, an oncologist or hematologist.

D. INITIAL CRITERIA FOR APPROVAL
1. Systemic light chain amyloidosis
   a. Authorization of 6 months may be granted for members prescribed Velcade as primary therapy 
      for the treatment of systemic light chain amyloidosis as monotherapy or in combination with 
      ANY of the following regimens:
      i. Monotherapy
      ii. Dexamethasone
      iii. Dexamethasone and melphalan
      iv. Dexamethasone and cyclophosphamide
iv. **Dexamethasone and melphalan**

2. **Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma**
   a. Authorization of 6 months may be granted for members prescribed Velcade for the treatment of Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma as monotherapy or in combination with ANY of the following regimens:
      - **Monotherapy**
        i. Dexamethasone
        ii. Rituximab
        iii. Dexamethasone and rituximab

3. **Active (symptomatic) multiple myeloma**
   a. Member has active myeloma defined as clonal bone marrow plasma cells ≥ 10% or biopsy-proven bony or extramedullary plasmacytoma AND any one or more of the following myeloma-defining events:
      i. Serum calcium level greater than 11.0 mg/dl or > 1 mg/dl higher than the upper limit of normal
      ii. Renal insufficiency (serum creatinine greater than 2 mg/dl or creatinine clearance < 40 ml/min)
      iii. Anemia (hemoglobin level less than 10 g/dl or > 2 g/dl below lower limit of normal)
      iv. Osteolytic bone lesions on X-ray, CT or PET-CT
      v. Clonal bone marrow plasma cells ≥ 60%
      vi. Abnormal serum free light chain (FLC) ratio ≥ 100 (involved kappa) or < 0.01 (involved lambda)
      vii. More than 1 focal lesion on MRI studies > 5 mm
   b. Authorization of 6 months may be granted for members prescribed Velcade as primary therapy for the treatment of multiple myeloma in patients who are eligible for stem cell transplant in combination with ANY of the following regimens:
      i. Dexamethasone
      ii. Dexamethasone and cyclophosphamide
      iii. Dexamethasone and doxorubicin
      iv. Dexamethasone and lenalidomide
      v. Dexamethasone and thalidomide
   b. Authorization of 6 months may be granted for members prescribed Velcade as primary therapy for the treatment of multiple myeloma in patients who are NOT eligible for stem cell transplant in combination with:
      i. Dexamethasone
      ii. Dexamethasone and cyclophosphamide
      iii. Dexamethasone and lenalidomide
      iv. **Melphalan and prednisone**
   c. Authorization of 6 months may be granted for members prescribed Velcade as maintenance therapy for the treatment of multiple myeloma as monotherapy
d. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of previously treated or relapsed multiple myeloma as part of ANY of the following regimens for patients who will NOT be receiving the same regimen as their primary chemotherapy regimen:

i. As monotherapy

ii. In combination with dexamethasone

iii. In combination with dexamethasone and lenalidomide

iv. In combination with dexamethasone and cyclophosphamide

v. In combination with dexamethasone and lenalidomide

vi. In combination with dexamethasone and thalidomide

vii. In combination with dexamethasone and bendamustine

viii. In combination with liposomal doxorubicin

ix. In combination with bortezomib, dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide (VTD-PACE)

e. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of previously treated or relapsed multiple myeloma as part of ANY of the following regimens in patients who will be receiving the same therapy as their primary chemotherapy, were transplant candidates, and the relapse occurred at least 6 months after their primary chemotherapy as part of ANY of the following regimens:

i. Dexamethasone

ii. Dexamethasone and cyclophosphamide

iii. Dexamethasone and doxorubicin

iv. Dexamethasone and lenalidomide

v. Dexamethasone and thalidomide

f. Authorization of 6 months may be granted for members prescribed Velcade as therapy for the treatment of relapsed multiple myeloma as part of ANY of the following regimens in patients who will be receiving the same therapy as their primary chemotherapy, were NOT transplant candidates, and the relapse occurred at least 6 months after their primary chemotherapy as part of ANY of the following regimens:

i. Dexamethasone

ii. Dexamethasone and cyclophosphamide

iii. Dexamethasone and lenalidomide

iv. Melphalan and prednisone

4. Mantle Cell Lymphoma
a. Authorization of 6 months may be granted for members prescribed Velcade for induction therapy for mantle cell lymphoma as part of the VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen

b. Authorization of 6 months may be granted for members prescribed Velcade for second-line therapy for mantle cell lymphoma with or without rituximab for relapsed, refractory, or progressive disease

5. Castleman’s Disease
a. Authorization of 6 months may be granted for members prescribed Velcade for the treatment of multicentric Castleman’s disease and Velcade will be used with or without rituximab as subsequent therapy for disease that has progressed following treatment of relapsed, refractory, or progressive disease.

E. CONTINUATION OF THERAPY

1. No previous authorization/precertification:
   All members (including new members and members currently receiving treatment without prior authorization) must meet criteria for initial approval in section D.

2. Reauthorization:
   Authorization of 6 months may be granted to members who are prescribed Velcade for continuation of therapy if Velcade was previously authorized by HMSA/CVS and there is evidence of a lack of disease progression on therapy and by supplying the following information:
   a. A current oncology note documenting the patient’s response to treatment showing no progression of disease
   b. Current laboratory reports (e.g., beta-2 microglobulin, serum free light chain assay, or serum immunoglobulin) or other objective measures showing no progression of disease when compared with previous results.
   All members, including new members, requesting authorization for therapy must meet ALL initial authorization criteria in section D.

Members who were previously approved for Velcade by HMSA may request reauthorizations after their initial approval. Approval for an additional 6 months may be granted if the following information is supplied and the member does not demonstrated evidence of disease progression:
- A current oncology note documenting the patient’s response to treatment showing no progression of disease
- Current laboratory reports (e.g., beta-2 microglobulin, serum free light chain assay, or serum immunoglobulin) or other objective measures showing no progression of disease when compared with previous results

F. DOSING AND ADMINISTRATION
   Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.
G. ADMINISTRATIVE GUIDELINES
Precertification is required. Please refer to the HMSA medical policy web site for the fax form.

H. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

I. REFERENCES

Document History
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